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13. ABSTRACT (Maximum 200 Words)

In this proposal, we hypothesize that inhibition of IGF action by IGFBP-1 will prevent breast cancer in a SV40 Tag transgenic model of breast cancer. We will test this hypothesis with two specific aims: 1) to inhibit IGF action at the mammary epithelial cell by creating transgenic mice that express IGFBP-1 under the control of the whey acidic protein (WAP) promoter and 2) to test the ability of IGFBP-1 to suppress tumorigenesis by mating these animals with C3/Tag transgenic mice.

To achieve these goals, we have created the expression vector, injected the construct into mice, and now have our first generation of mice. Of the animals we have analyzed, approximately 25% have the transgene. We are currently in the process of mating the F1 generation and determining if we have achieved IGFBP-1 expression in the mammary gland.

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INTRODUCTION

In this proposal, we hypothesize that inhibition of IGF action by IGFBP-1 will prevent breast cancer in a SV40 Tag transgenic model of breast cancer. We will test this hypothesis with two specific aims: 1) to inhibit IGF action at the mammary epithelial cell by creating transgenic mice that express IGFBP-1 under the control of the whey acidic protein (WAP) promoter and 2) to test the ability of IGFBP-1 to suppress tumorigenesis by mating these animals with C3/Tag transgenic mice.

BODY

Specific Aim (Task) #1 - To inhibit IGF action at the mammary epithelial cell by creating transgenic mice that express IGFBP-1 under the control of the whey acidic protein (WAP) promoter

a. Months 0-3 -   Create WAP-IGFBP-1 transgene vector

We have cloned the IGFBP-1 into the appropriate expression vector in animals.

b. Months 3-9 -   Create and identify IGFBP-1 F1 progeny

The transgene construct was injected into embryos. Of the 12 animals initially identified, approximately 25% (3 animals) had incorporated the transgene as detected by Southern blot analysis of tail vein DNA. We have spent some time trying to use PCR as a screening method. At this point in time, we are unable to determine the appropriate conditions to use PCR, so we are now relying on Southern blots.

c. Months 9-16 -   Characterize level of IGFBP-1 expression in mammary gland, determine influence of IGFBP-1 expression on lactation, examine activation of IGFR1

We have learned the technique of mammary gland dissection (on non-transgenic animals) and have also received advice on the obtaining milk from mice. At present, we are breeding our founders and have not yet analyzed levels of IGFBP-1 protein expression in the milk or mammary gland. We believe that this goal will be accomplished in the next several months.

Specific Aim (Task) #2 - To test the ability of IGFBP-1 to suppress tumorigenesis by mating these animals with C3/Tag transgenic mice

We have not yet begun work on this aim.

KEY RESEARCH ACCOMPLISHMENTS

- ◆ Created the WAP-IGFBP-1 expression construct

- ◆ Generated founder mice with integration of the construct

REPORTABLE OUTCOMES

None.

CONCLUSIONS

We have generated the appropriate construct and now have founder mice. We hope that IGFBP-1 will be expressed at high levels and these animals can be used to test the hypothesis that inhibition of IGF signaling will prevent breast cancer.

REFERENCES

None

APPENDICES

None